



## Antibiotics for UTIs in Elderly Patients: Too Little, Too Late?

Not giving antibiotics to—or delaying them in—elderly patients with a urinary tract infection (UTI) can significantly increase the risk of bloodstream infection and death within 60 days, according to researchers from the UK's Imperial College London, St. George's, University of London, and King's College London.

The researchers looked at primary care records linked to hospital-episode statistics and death records for 157,264 adults aged 65 years or older with at least one diagnosis of suspected or confirmed lower UTI. The average was two UTIs per patient.

Patients older than 85 years, who lived in a deprived area, and who had a high comorbidity index were mainly managed with deferred antibiotics or no antibiotics. Patients aged between 65 and 74 years were mainly prescribed immediate antibiotics. Most patients who received antibiotics were given trimethoprim or nitrofurantoin.

Overall, 7.5% of the UTI episodes involved at least one of a range of specific or nonspecific signs or symptoms within 30 days before the index UTI. The most common were pain, dysuria, micturition frequency, incontinence, and hematuria; 90% of patients with those symptoms were prescribed antibiotics. Patients with nonspecific signs, such as confusion and malaise, were much less likely to receive timely antibiotics.

Of 312,896 UTI episodes, 22,536 (7.2%) had no record of antibiotics being prescribed and 19,292 (6.2%) showed a delay in prescribing. Within 60 days, 1,539 patients had developed a bloodstream infection.

Compared to patients in the immediate-antibiotics group, patients in the deferred-antibiotics group were seven times more likely and those in the no-antibiotics group eight times more likely to develop a bloodstream infection within 60 days.

Also, patients in the no-antibiotics group were more than twice as likely to die and those in the deferred-antibiotics group 1.16 times more likely to die within 60 days of the UTI, compared to patients in the immediate-antibiotics group. Men older than 85 years were particularly at risk for both bloodstream infection and 60-day all-cause mortality.

The question remained, the researchers said, as to why so many vulnerable older patients were diagnosed with UTI but not prescribed antibiotics. It could be patient or physician choice, but it might be a response to the “culture of more judicious antibiotic use.” In addition, noted the researchers, antibiotic use is associated with the risk of *Clostridium difficile* infection in older people.

If, however, the reason is that the symptoms are “too mild,” the researchers say that patients with disease not severe enough for prompt antibiotic treatment are at risk of severe consequences. They advise starting antibiotics for UTI early in older high-risk patients, especially men older than 85 years.

Source: *BMJ*, February 27, 2019

## Opioid Prescriptions: For Most Pain, a Week is Enough

An opioid prescription for seven days or less is generally enough for most patients with acute pain, an FDA-supported study suggests.

Researchers from Brigham and Women's Hospital and Harvard Medical School analyzed data on 176,607 patients who visited a primary care setting for an episode of acute pain. They divided prescriptions according to 10 conditions: joint pain, back pain with and without radiculopathy, headache, neck pain, tendonitis/bursitis, muscle strain/sprain, nephrolithiasis, musculoskeletal injury, and dental pain.

Overall, 13,440 (7.6%) of patients filled an opioid analgesic prescription within seven days of the initial visit. Among those patients, the median initial amount filled across conditions ranged from four to seven days, 20 to 30 tablets or capsules, and 100 to 155 morphine milligram equivalents. Approximately 2,400 patients who were dispensed an opioid analgesic obtained at least one refill within 30 days of the initial prescription.

More men than women got refills (19.3% vs. 15.8%). Patients also were more likely to get refills if they had a recent history of using gabapentin (28.3%), benzodiazepines (26.5%), or sedative hypnotics (20%).

For an initial seven-day prescription, refill probability ranged from 11% for headache to 41% for musculoskeletal injury. Among all patients who received an initial prescription, fewer than one in five obtained a refill. The probability of a refill appeared to decline with increasing initial prescription duration for some conditions (back pain with radiculopathy, nephrolithiasis, and dental pain). For other conditions, the probability remained relatively constant regardless of the amount initially prescribed.

The researchers say that, for the purposes of their study, refills within 30 days were presumed to be for treatment of the same pain condition as the initial filling, although they could not directly link the diagnostic and prescription claims to verify this. They also note that although male sex, recent use of benzodiazepines, and other patient characteristics were associated with higher refill rates, such factors should be interpreted with caution as they might also be associated with conditions requiring longer treatment.

Source: *MMWR*, 68:6, February 15, 2019

## HHS Updates Decontamination Guidance With New Research

With help from researchers from the University of Hertfordshire in the UK, the Department of Health and Human Services has updated their guidance on how best to decontaminate after mass chemical exposure. This second edition of *Primary Response Incident Scene Management* (PRISM, [www.medicalcountermeasures.gov](http://www.medicalcountermeasures.gov)) incorporates new scientific evidence on emergency self-decontamination, hair decontamination, and the interactions of chemicals with hair.



The goal of working with the University of Hertfordshire was to help emergency managers and first responders make “fundamental and fast decisions on how to save the greatest number of lives in chemical emergencies,” says Rick Bright, PhD, director of the Biomedical Advanced Research and Development Authority (BARDA).

The study included a large-scale exercise in which more than 80 volunteers were dosed with a chemical warfare agent simulant to quantify the efficacy of different forms of decontamination.

Notably, the research demonstrates that immediate “dry” decontamination—wiping down the victim with any absorbent material (e.g., toilet paper, paper towels, or wound dressings) can be highly effective on its own, and can be carried out by affected individuals themselves under the instruction of first responders. The dry decontamination step removes up to 99% of contamination and minimizes the accumulation of hazardous material in the subsequent steps.

The new guidance also expands on the effects of the “triple protocol,” a combined decontamination strategy. The three steps of that protocol—dry decontamination, wet decontamination using water deluges from fire trucks, and technical decontamination—have been shown to remove 99.9% of chemical contamination. Moreover, the latest clinical evidence indicates that the three-step approach is faster and more effective than traditional methods for treating chemically contaminated patients.

The guidelines also address how communities can prepare for chemical emergencies, and what to do after the event, such as providing washcloths, towels, blankets, and temporary clothing.

Federal experts and the researchers devised the Algorithm Suggesting Proportionate Incident Response Engagement (ASPIRE), a decision-support tool to help emergency management planners and responders decide which decontamination approach best suits a given situation. Using ASPIRE, they can tailor plans and responses based on the chemical and type of exposure, how quickly the chemical evaporates, and the amount of time passed since exposure.

ASPIRE and the guidance are integrated into Chemical Hazards Emergency Medical Management (CHEMM), a web-based resource and suite of preparedness and emergency response tools. The developers also plan to incorporate them into an app.

Sources: HHS.gov, February 21, 2019; University of Hertfordshire, October 19, 2018

## For 20+ Years, Pain Has Been on the Rise

Pain is becoming a fact of life for greater numbers of people, and more people are turning to opioids to treat it, according to a survey sponsored by the National Center for Complementary and Integrative Health.

Researchers looked at approximately two decades-worth of cumulative data from the Medical Expenditure Panel Survey

(MEPS) and found that since 1997–1998, pain prevalence in U.S. adults rose by 25%.

In 1997–1998, approximately 33% of American adults had at least one painful health condition. In 2013–2014, the proportion was 41%. For close to 68 million people, moderate to severe pain was interfering with normal work activities. And those people were turning more often to strong opioids—e.g., fentanyl, morphine, oxycodone—for help. The use of opioids to manage pain more than doubled in just 10 years: from 4.1 million (11.5%) in 2001–2002 to 10.5 million (24.3%) in 2013–2014.

People with severe pain-related interference were also more likely to have had four or more opioid prescriptions and to have visited a doctor’s office six or more times for pain, compared to people with minimal pain-related interference.

Opioid use peaked between 2005 and 2012, but since 2012, opioid use has slightly declined. The researchers say this ties in with a reduction in the use of weak opioids and in the number of patients reporting only one opioid prescription.

The survey also found some small downward shifts in health care visits. Ambulatory office visits plateaued between 2001–2002 and 2007–2008, and decreased through 2013–2014. In addition, there were small but statistically significant drops in pain-related emergency room visits and overnight hospital stays.

The researchers say their findings suggest that more education about the risk–benefit ratio of opioids “appears warranted.”

Sources: NIH.gov, February 13, 2019; *The Journal of Pain*, January 15, 2019

## Brain Biomarkers May Help Explain Severe PTSD Symptoms

Some people undergo a traumatic event and have few side effects. Others may suffer greatly, and for a long time. Why?

A current theory holds that during a traumatic event, a person may learn to associate the people, locations, and objects in the situation with the trauma, and long after the event even the “safe” stimuli can trigger fearful and defensive responses. Experts believe it’s an “overlearned response” to a threatening experience. But the way in which that learning happens is not well understood, say researchers from Yale University and Mount Sinai. Their study, however, may shed new light on how people with PTSD symptoms learn and unlearn fear.

In the study, funded in part by the National Institute of Mental Health, the researchers examined how the mental adjustments performed during learning, and the way in which the brain tracks these adjustments, relate to symptom severity.

They gave combat veterans with varying levels of PTSD symptom severity a reversal learning task. Participants were shown two mildly angry human faces and received a mild shock after viewing one face, but not the other. Then the task was reversed, with the aim of having the participants “unlearn” their original fear conditioning and testing their ability to relearn



how to respond to negative surprises in the environment.

Although all participants were able to perform the reversal learning, the researchers found “pronounced differences in the ‘learning rates.’” Highly symptomatic veterans tended to overreact when what they expected to happen and what actually happened didn’t match up.

The researchers say they found biomarkers that could explain the different reactions. In the highly symptomatic veterans, two areas of the brain—the amygdala and striatum—were less able to track changes in the threat level.

“One’s inability to adequately adjust expectations for potentially aversive outcomes has potential clinical relevance,” said Ilan Harpaz-Rotem, PhD, co-leader of the study, “as this deficit may lead to avoidance and depressive behavior.”

The researchers say their findings could give a “more fine-grained understanding of how learning processes may go awry in the aftermath of combat trauma.”

Sources: NIH, January 28, 2019; Yale School of Medicine, January 22, 2019

## When a Public Health Alert Goes Wrong

At 8:07 AM on January 13, 2018, people in Hawaii received an emergency alert advising them to seek shelter from an incoming ballistic missile.

A very long 38 minutes later, the message was retracted via the same systems that had sent it—the Wireless Emergency Alert system, which sends location-based warnings to wireless carrier systems, and the Emergency Alert System, which sends television and radio alerts.

The Federal Communications Commission report that covered the debacle noted that, among other errors, the employee responsible for triggering the false alert believed the missile threat was real. Moreover, the exercise plans did not document a process for disseminating an all-clear message. And on top of that, the established ballistic-missile alert checklist did not include a step to notify the local public information officer responsible for communicating with the public, media, other agencies, and other stakeholders during an incident.

Researchers from the CDC and Hawaii Department of Health analyzed tweets sent during two periods: early (8:07–8:45 AM), the 38 minutes during which the alert circulated; and the late period (8:46–9:24 AM), 38 minutes after the correction had been issued.

They found that four themes dominated the early period: information processing, information sharing, authentication, and emotional reaction (shock, fear, panic, and terror). Information processing was defined as any indication of initial mental processing of the alert. Many of the tweets dealt with coming to terms with the threat.

During the late period, information sharing and emotional reaction persisted, but they were joined by new themes that, according to the researchers, were “fundamentally different”

from the early-period themes, and reflected reactions to misinformation: denunciation, insufficient knowledge to act, and mistrust of authority. “Insufficient knowledge to act” involved reacting to the lack of a response plan, particularly not knowing how to properly take shelter. Denunciations blamed the emergency warning and response, especially the time it took to correct the mistake. Mistrust of authority involved doubting the emergency alert system or governmental response.

How can a situation like this be better handled? The researchers say public health messaging during an emergency is complicated. For instance, it’s influenced by how messages are perceived and interpreted by different people, and by the fact that messages need to be sent over multiple platforms to ensure that the information is disseminated accurately and quickly.

This is why social media is both a handicap and a boon in public health emergencies. Tweets spread misinformation as fast as information (if not faster), so the first messages are critical. In addition to conveying timely messages, the researchers advise, public health authorities need to address the reactions during each phase of a crisis. They also need to establish credibility to prevent the public from mistrusting the public health message and its issuers.

Most importantly, perhaps, alerts should carry clear instructions for persons in the affected area to carry out during an emergency.

Source: *MMWR*, 68:7, February 22, 2019

## Universal ‘Test-and-Treat’ Strategy Cuts Down New HIV Infections

The largest HIV prevention study conducted to date found that house-to-house HIV testing and providing immediate treatment referrals for everyone testing positive resulted in markedly reduced new HIV infections. The findings suggest that a universal “test-and-treat” strategy could be “an important addition to our toolbox of proven HIV prevention modalities,” said Anthony Fauci, MD, director of the National Institute of Allergy and Infectious Diseases (NIAID).

The NIAID-sponsored study, Population Effects of Antiretroviral Therapy to Reduce HIV Transmission (PopART), was conducted from 2013 to 2018 in 21 urban and peri-urban communities in Zambia and South Africa, each with roughly 50,000 residents.

The communities were grouped as seven “triplets” matched by geographical location and estimated HIV prevalence. The first group received annual house-to-house voluntary HIV testing and counseling, linkage to care for those testing positive, and the offer of a suite of proven prevention measures for those who tested negative. The second group received the same services as the first, except treatment was offered according to national guidelines. The third group served as a control, and received HIV prevention and testing services according to the local standard of care and HIV treatment according to



national guidelines.

At the start of the study, the national guidelines for HIV treatment in Zambia and South Africa specified starting ART when the CD4+ T-cell count had declined to 350 cells/ $\mu$ L. In 2014, that threshold was raised to 500 cells/ $\mu$ L. In 2016, both countries recommended that everyone diagnosed with HIV begin ART immediately regardless of CD4+ T-cell count. Consequently, the first and second groups received the same intervention during the last two years of the study.

The researchers also recruited a random sample of about 2,300 adults from each community, and visited them once a year for three years to collect data and test blood.

In the first three years, during nearly 40,000 person-years of follow-up, 553 people developed HIV infection (1.4 infections

per 100 person-years). HIV incidence was 7% lower in group 1 than in the control group, although the difference was not statistically significant. However, HIV incidence was 30% lower in group 2 compared to the control group—a highly statistically significant and consistent result. (The researchers can't yet explain why new HIV infections did not decline in all the communities where people who tested positive were offered immediate treatment.)

Of participants who tested positive by year 2, 72% of group 1, 68% of group 2, and 60% of the control group had achieved viral suppression.

Source: NIH.gov, March 5, 2019 ■